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| EXAMINER | |
|---|---|
| SITTON, JEHANNE SOUAYA | |
| **ART UNIT** | **PAPER NUMBER** |
| 1634 | |

DATE MAILED: 01/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/786,011 | SCHEU ET AL. | |
| | Examiner | Art Unit | |
| | Jehanne Souaya Sitton | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *03 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-5,7-12 and 14-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-12 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

1. Currently, claims 1-5, 7-12 and newly added claims 14-16 are pending in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. Any rejections not reiterated are hereby withdrawn in view of the amendments to the claims filed in the response dated November 3, 2003. The following rejections are newly applied as necessitated by the amendment filed 11/3/2003. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *New Grounds of Rejection*

### *Claim Rejections - 35 USC § 112*

3. Claims 1-2, 4-5, 7-11, and newly added claims 14-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER Rejection.

The claims have been amended to recite nucleic acid molecules which are identical to at

least 17 successive nucleotides of any one of SEQ ID NOS 1-7 and fragments of 17 to 250 or 17-30 nucleotides. However, the specification provides no support for fragments of 17 up to unlimited upper lengths of any of SEQ ID NOS 1-7, 17 mer fragments of SEQ ID NO: 1 or 3-7, or fragments of 17-250 or 17-30 nucleotides of SEQ ID NOS 1-7. The specification teaches the specific sequences of SEQ ID NOS 1-7 and contemplates that probes and primers of the invention are 10-250 or 15-30 nucleotides in length (page 6). The specification, however provides no basis for fragments of 17 up to unlimited upper lengths of any of SEQ ID NOS 1-7, 17 mer fragments of SEQ ID NO: 1 or 3-7, or fragments of 17-250 or 17-30 nucleotides of SEQ ID NOS 1-7.

In addition, claim 1 has been amended to specifically recite 90% identity, however, the specification does not teach or contemplate sequences with a % identity to any of SEQ ID NOS 1-7, nor does the specification specifically define the term "homology" to encompass such. Therefore, there is no support in the specification for sequences with a % identity to any of the SEQ ID NOS 1-7.

4. Claims 1-2, 4-5, 7-12 and newly added claims 14-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to fragments of 17 up to unlimited upper lengths (claim 1) of any of SEQ ID NOS 1-7, fragments of 17-250 (claim 2) or 17-30 (claim 16) nucleotides of SEQ ID

NOS 1-7 as well as methods of using such sequences to detect Listeria monocytogenes and kits comprising such sequences. The specification teaches the specific sequences of SEQ ID NOS 1-7 and teaches that such sequences correspond to specific positions of the mpl gene taught by Domann et al (1991). The claims, however, are drawn to nucleic acids comprising fragments from within the recited SEQ ID NOS which can include any nucleotide sequences on either side of the fragments, as well as methods of using such. These sequences encompass mutants, variants, and homologs of the recited SEQ ID NOS which have not been taught or described by the specification. The single sequence of the mpl gene is not representative of the large genus of variants, mutants and homologs encompassed by the claim. The specification only teaches the specific sequences of SEQ ID NOS 1-7 and teaches that they are identical to certain positions of the mpl sequence taught in the art. The specification provides no teaching or guidance of fragments of mutants, variants, or homologs of the mpl gene or methods of using such to detect Listeria monocytogenes.

Additionally, claim 12 is drawn to a method of distinguishing Listeria monocytogenes by using one of the nucleic acid molecules of claim 3. Claim 3, however, is drawn to fragments from within the recited SEQ ID NOS, and the specification has not taught or described how many nucleotides of the recited SEQ ID NOS are required for specificity to Listeria monocytogenes. For example, the claims encompass a 3mer or a 10mer nucleic acid sequence, which would be expected to occur thousands of times in any bacterial genome, however the specification has not taught what fragments from within the recited SEQ ID NOS are specific for Listeria monocytogenes. Further, claim 12 recites detecting differences in genomic DNA or RNA in at least one nucleotide position in the region of one of the nucleic acids of claim 3,

however the specification does not teach what single nucleotides position changes distinguish Listeria monocytogenes from other bacteria.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOS: 1-7, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

5. Claims 1-5, 7-12 and 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite as the recitation of "identical to" makes it is unclear if the claim is drawn only to 17 mer (consecutive nucleotide) fragments from within the recited SEQ ID NOS or if they are meant to encompass larger sequences with any sequence on either side of the 17mer fragment. The use of the word "identical to" appears to encompass the former case, however the dependency of claim makes such unclear. It is further noted that if the former is the case, claim 2 does not further limit claim 1.

Amended claim 3 is indefinite as it is unclear if the recitation of "*An* isolated nucleic acid molecule *of*" intends the claim to encompass only a nucleic acid consisting of any one of SEQ ID NOS 1-7, or the complements thereof, or whether the claim encompass fragments from within any of SEQ ID NOS 1-7.

Amended claim 5 is indefinite as it is unclear what "modifications" are encompassed by the claim. "A manner known per se" does not make clear to what extent, modifications could be made to the claimed nucleic acids and still be encompassed by the claims.

Claims 9 and 12 are indefinite as it is unclear what the method steps comprise. For example, the methods recite "providing at least one nucleic of claim 1 [or claim 3]" and "detecting [or distinguishing]…". However, it is unclear how the step of detecting [or distinguishing] comes about from merely "providing a nucleic acid". It is unclear if the nucleic

acid in the 'providing step' is being detected or is used in the next step of 'detecting [or distinguishing]. Further, in claim 12, it is unclear what sequences are being compared to be able to discern "differences in the genomic DNA and/ or RNA in at least one nucleotide position in the region of one of the nucleic acid molecules of claim 3". In other words, does one provide a sequence in step b from the test sample in step a and then determine if it is different to some sequence (that 'some sequence' being unclear), or is the nucleic acid of step b being compared to the test sample of step a? Likewise, in claims 10 and 11, which depend from claim 9, it is unclear if the hybridization or amplification is used to obtain the nucleic acid from claim 1 or if the nucleic acid from claim 1 is used for hybridization or amplification.

***Claim Rejections - 35 USC § 102***

6. Amended claims 1, 4, 5, 7, 9, 10, and newly added claims 14 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Domann.

Due to the dependency of claim 2, claim 1 has been broadly interpreted to contain no upper length limitation. As such, the claim encompasses sequences with a minimum of 17 sequences of any of SEQ ID NOS 1-7 as well as sequences on either side. As Domann et al teach the complete sequence of the mpl gene, and SEQ ID NOS 1-7 are found within the mpl gene, the isolated mpl gene taught by Domann anticipates the claimed nucleic acid molecule. Domann et al further teach a method of specifically detecting L. monocytogenes using a probe (page 66, para bridging cols 1 and 2) to the mpl coding sequence (see page 68, para bridging cols 1 and 2, and Fig. 7). Domann et al teach that this probe did not give a positive result with 3 other species of Listeria.

7. Claims 1, 2, 4, and 5 rejected under 35 U.S.C. 102(b) as being anticipated by EST Accession number AA207653 (March 1997).

Due to the dependency of claim 2, claim 1 has been broadly interpreted to contain no upper length limitation. As such, the claim encompasses sequences with a minimum of 17 sequences of any of SEQ ID NOS 1-7 as well as sequences on either side. Accession number AA207653 teaches a 152 base pair sequence (claim 2, 17-250 nucleotides) which is identical at positions 51-67 to the complement of positions 3-19 of SEQ ID NO: 7 ("17 successive nucleotides" - alignment provided).

8. Amended claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by Brennan et al (US Patent 5,474,796).

Brennan teaches an array of isolated trimers (see Fig. 1b). The claim has been broadly interpreted to encompass fragments from within the SEQ ID NOS. The trimers taught by Brennan are fragments from within the recited SEQ ID NOS. Note: this rejection can be easily overcome by reciting: "An isolated nucleic acid molecule from the group consisting of SEQ ID NO: 1…".

***Claim Rejections - 35 USC § 103***

9. Amended claims 2, 3, 9, 11-12 and newly added claim 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Domann et al in view of Rossen et al.

Domann et al teach a nucleic sequence which encodes a metalloprotease gene from listeria monocytogenes which is immediately downstream of the listeriolysin gene. Domann et al teach the nucleotide sequence of this gene and also teach an alignment of the polypeptide

encoded by the gene with other metalloprotease genes from other organisms (Figs 1 and 2) and teaches that this gene is unique to L. monocytogenes (see abstract, page 68, para bridging cols 1 and 2). Domann et al further teach a method of specifically detecting L. monocytogenes using a probe to the mpl coding sequence (see page 68, para bridging cols 1 and 2, and Fig. 7). Domann et al teach that this probe did not give a positive result with 3 other species of Listeria. Although Domann et al do not teach a method of detecting L. monocytogenes using primers to the mpl sequence or probes up to 250 or 30 nucleotides Rossen et al teach detecting L. monocytogenes using primers to a sequence downstream of the hlyA gene, which is known to be unique to L. monocytogenes. Rossen et al teach that primer M14 was specific for L. monocytogenes.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of detecting L. monocytogenes of Domann et al to construct primer sequences to detect L. monocytogenes as taught by Rossen for the purpose of detecting the harmful pathogen in food samples. The ordinary artisan would have been motivated to do so because Rossen et al teaches the need for such assays and only teaches a single primer that was specific for L. monocytogenes. While Rossen et al do not teach specific sequences for such purposes, Rossen et al do teach a specific region within the Listeria genome that can be used to construct such sequences. As Domann et al teach that a gene specific for L. monocytogenes exists downstream from the hemolysin gene, the ordinary artisan would have been motivated to use sequences from the mpl gene taught by Domann et al to detect Listeria monocytogenes. The ordinary artisan would have further been motivated to use sequences from the mpl gene to construct species specific primers because Domann et al teach that the mpl gene

is specific to L. monocytogenes. Thus the ordinary artisan would have expected, from the teachings of Domann et al, that such primers could be constructed from the mpl gene.

The responses arguments as they pertain to the newly cited rejection above (starting on page 11, 3rd para), will be addressed. The response asserts that Rossen does not teach the sequence of the oligonucleotide primers. This argument is not persuasive because the rejection is not set forth with regard to the specific primer sequences of Rossen et al but rather that Rossen provides motivation to detect L. monocytogenes with primers. The response further asserts that Rossen et al teach a primer that is not specific but that all the primers of the instant application were specific for L. monocytogenes. The response asserts that "obvious to try" is not the standard for a 103 rejection and that the primers of the instant application provided unexpected results as seen on page 5 of the specification. These arguments have been thoroughly reviewed but were not found persuasive for the following reasons. The teachings of Domann et al and Rossen et al provide the ordinary artisan with a reasonable expectation of success that L. monocytogenes specific primers and probes could be constructed. Rossen et al teach of the ability to construct one such primer (LM14) and Domann et al teach that the mpl gene is specific to L. monocytogenes and teaches of the ability to construct species specific probes. Given the high state of the art at the time of the instant application with regard to constructing species specific probes and primers to sequences that the art designates as species specific, there was a high expectation of success that probes and primers to the mpl gene could be constructed that were species specific. However, it would also be expected given lengths of probes and primers, GC content, degree of complementarity, hybridization conditions, etc that some sequences would not be specific for L. monocytogenes. Therefore, the assertion that the specific sequences of the

instant application gave unexpected results would be persuasive if the scope of the claims and the scope of the unexpected results were the same. The unexpected results mentioned in the response and in the specification are with regard to nucleic acid molecules consisting of the specific sequences of any of SEQ ID NOS 1-7, not fragments of them, not nucleic acids with sequences on either side, not nucleic acid molecules "comprising" fragments, not sequences with 90% identity or homology, however all of the claims continue to encompass a broader scope of nucleic acids than those that exhibited the unexpected results. Likewise, given GC content of nucleic acid molecules, length of nucleic acid molecules, degree of complementarity, etc, sequences that are fragments, nucleic acids with sequences on either side, nucleic acid molecules "comprising" fragments, and sequences with 90% identity or homology with SEQ ID NOS 1-7 would be expected to exhibit different properties than the specific sequences of SEQ ID NOS 1-7. The MPEP specifically states:

> **716.02(d) [R-1] Unexpected Results Commensurate in Scope With Claimed Invention**
> Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the "objective evidence of nonobviousness must be commensurate in scope with the claims which the evidence is offered to support." See > In re Peterson, 315 F.3d 1325, 1329-31, 65 USPQ2d 1379, 1382-85 (Fed. Cir. 2003) (data showing improved alloy strength with the addition of 2% rhenium did not evidence unexpected results for the entire claimed range of about 1-3% rhenium);< In re Grasselli, 713 F.2d 731, 741, 218 USPQ 769, 777 (Fed. Cir. 1983) (Claims were directed to certain catalysts containing an alkali metal. Evidence presented to rebut an obviousness rejection compared catalysts containing sodium with the prior art. The court held this evidence insufficient to rebut the prima facie case because experiments limited to sodium were not commensurate in scope with the claims.).

It is noted that the rejection has not been applied with regard to sequences consisting of the specific sequences of SEQ ID NOS 1-7.

10. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over unpatentable over Domann et al in view of Rossen et al, as applied to claims 2-3, 9, 11-12, and 16 above, and further in view of Ahern et al.

The teachings of Domann et al in view of Rossen et al are outlined above. Domann et al in view of Rossen et al do not teach primers in kit format, however, Ahern teaches that buying premade reagents and kits are convenient, therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to provide the primers of Domann et al in view of Rossen et al, in kit format as taught by Ahern, for the improvement of providing the primers of Domann et al in view of Rossen et al in a convenient format. The ordinary artisan would have been motivated to provide the primers of Domann et al in view of Rossen et al in kit format because Ahern teaches that providing reagents necessary for analysis in kit format are convenient.

***Conclusion***

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. No claims are allowable over the cited prior art.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0572. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

Note: The examiner's name has changed from Jehanne Souaya to Jehanne Sitton. All future correspondence to the examiner should reflect the change in name.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (571) 272-0507.

Jehanne Sitton

Jehanne (Souaya) Sitton
Primary Examiner
Art Unit 1634

1/15/04